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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
FORMAN, B	

ART UNIT	PAPER NUMBER
1655	13

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/394,230	GUNDERSON ET AL.	
	Examiner	Art Unit	
	BJ Forman	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 March 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. This action is in response to the request for reconsideration filed 7 March 2001 in Paper No. 12. The previous rejections in the Office Action of Paper No. 9 dated 1September 2000 n are maintained. All of the arguments have been thoroughly reviewed and are discussed below.

Applicant is reminded that changes to 37 C.F.R. § 1.121 require applicant to submit a clean set of all pending claims in addition to the marked up version of the amended claims.

Currently claims 1-18 are under prosecution.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cantor et al. (U.S. Patent No. 5,631,134, filed 5 June 1995) in view of Yershov et al. (Proc. Natl. Acad. Sci., USA, 1996, 93: 4913-4918).

Regarding Claim 1, Cantor et al. teach a method of determining the presence of a mutation in a target polynucleotide comprising the steps of providing a polynucleotide probe array wherein each probe comprises a double strand region and a single stranded n-mer overhang region; hybridizing a target polynucleotide to said overhangs in the array to generate a target hybridization pattern; and determining the presence of a mutation in the target polynucleotide by analyzing hybridization patterns (Column 8, lines 1-12) wherein the probes

are designed to identify mutations (Column 4, lines 5-8) comprising complete n-mer arrays (Column 12, lines 9-19). Cantor et al. do not teach hybridizing a reference polynucleotide to a second array and determining the presence of a mutation by comparing the reference and target hybridization patterns. However, the comparison of reference and target hybridization patterns to determine the presence of a mutation was known and routinely practiced in the art at the time the claimed invention was made. Specifically, Yershov et al. teach a similar method for determining the presence of a mutation in a target polynucleotide comprising hybridizing a target polynucleotide to one array and a reference polynucleotide to a second array and determining the presence of a mutation by comparing reference and target hybridization patterns (page 4916, Fig. 3). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Cantor et al. with the teachings of Yershov et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to modify the hybridization analysis of Cantor et al. with the comparison and analysis of Yershov et al. for the expected benefit of simplified diagnostics with enhanced reliability as taught by Yershov et al. (Abstract, last 4 lines).

Regarding Claim 2, Cantor et al. teach the hybridized polynucleotide is ligated to the probe (Column 8, lines 8-9).

Regarding Claim 3, Cantor et al. teach the hybridized polynucleotide is ligated to the probe (Column 8, lines 8-9). Cantor et al. do not discuss the reference polynucleotide. However, reference polynucleotides were known to one of ordinary skill in the art as discussed above and the skilled practitioner would have known that for comparison purposes, a target and reference polynucleotide would be treated equally i.e. ligated to the probe.

Regarding Claim 4, Cantor et al. teach the overhangs have free 5' ends (Column 12, lines 46-49 and Fig. 1B).

Regarding Claim 5, Cantor et al. teach the overhangs have free 3' ends (Column 12, lines 38-45 and Fig. 1A).

Regarding Claim 6, Cantor et al. teach the n-mer comprises from about 4 to 50 nucleotides (Column 12, lines 57-60).

Regarding Claims 7-9, Cantor et al. teach the mutation is a single nucleotide mutation (Column 10, lines 38-40). Cantor et al. do not teach the single nucleotide mutation is a substitution (Claim 7), a deletion (Claim 8) and a insertion (Claim 9). However, one skilled in the art at the time the claimed invention was made would have known that the single nucleotide mutations taught by Cantor et al. include the claimed substitution, deletion and insertion mutations.

Regarding Claim 10, Cantor et al teach the method wherein single nucleotide mutations are identified wherein the identification quickly, efficiently and easily detects inherited mutations which cause disease and DNA depended phenotype and somatic variations (Column 10, lines 38-45). Cantor et al. do not teach the target polynucleotide is selected from the recited sequences. However, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Cantor et al. with the teachings of Cantor et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to apply the mutation detection teaching of Cantor et al. to sequences known to contain single nucleotide mutations for the obvious benefit of detecting clinically relevant mutations quickly, efficiently and easily as taught by Cantor et al.

Regarding Claim 11, Yershov et al. teaches the arrays are arranged in parallel (page 4916, left column, second full paragraph).

Response to Arguments

4. Applicant argues that the invention of Claim 1 which provides at least two identical arrays wherein each constitutes a complete set of n-mers to determine the presence of a mutation in a target polynucleotide by comparing a reference and target hybridization pattern

is not prime facie obvious over the teaching of Canter et al. alone or in view of Yershov et al. because Canter et al. teach the array comprising complete n-mers for determining a nucleotide sequence by hybridization but do not teach determining the presence of a mutation by comparing hybridization patterns and because Yershov et al. teach "examination of DNA from.... patients" on chips (i.e. comparing hybridization patterns) but they do not teach probe arrays comprising a complete set of n-mers to analyze mutations. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Cantor et al. teach a polynucleotide array wherein each probe comprises a double stranded region and a single stranded overhang region such that the overhangs in each array constitute a complete set of n-mers (Column 5, line 56-Column 6, line 5) wherein the hybridization pattern is analyzed (Column 7, lines 14-18) and wherein the arrays are used for determining the presence of a mutation (Column 10, lines 30-47) and Yershov et al. teach providing at least two identical probe arrays and comparing the hybridization pattern of a target polynucleotide and a reference polynucleotide to determine the presence of a mutation (i.e. β-thalassemia mutations, Fig. 3). Therefore, It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the comparison of hybridization patterns to detect a mutation as taught by Yershov et al. to the hybridization array taught by Cantor et al. for the expected benefit of quickly, easily and accurately identifying a mutation or variations as taught by Cantor et al. (Column 4, lines 5-8).

Applicant further argues that the instant method can be used to determine two or more unknown polynucleotides without having to know the sequence of one of the polynucleotides and one may determine mutations in a target polynucleotide without sequencing the target polynucleotide. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., sequence and mutation identification without sequencing) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The instant claims are drawn to methods of determining the presence of a mutation and determining whether two or more target polynucleotides are identical. The claims do not recite limitations which exclude sequencing. Additionally, the open claim language "comprising" encompasses the extra steps of Canto et al. and Yershov et al.

5. Regarding Claim 12, Cantor et al. teach a method of determining relatedness two or more polynucleotides comprising the steps of providing a polynucleotide probe array wherein each probe comprises a double stranded region and a single stranded n-mer overhang region such that the over hangs in each array constitute a complete set of n-mers; hybridizing a target polynucleotide to said overhangs in the array to generate a hybridization pattern and analyzing the hybridization patterns (Column 8, lines 1-10). Cantor et al. do not teach the method comprising two identical arrays wherein the target polynucleotide is hybridized to one array and a second target polynucleotide is hybridized to a second array. However, the comparison of hybridization patterns to determine if two or more sequences are identical was known and routinely practiced in the art at the time the claimed invention was made. Specifically, Yershov et al. teach a similar method for determining whether two or more polynucleotides are identical comprising hybridizing a target polynucleotide to one array and a second target polynucleotide to a second array and determining the presence of a mutation by comparing reference and target hybridization patterns (page 4916, Fig. 3). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the method of Cantor et al. with the teachings of Yershov et al. to obtain the claimed invention because the skilled practitioner in the art would have been motivated with a reasonable expectation of success to modify the polynucleotide identification of Cantor et al. with the comparison of polynucleotides as taught by Yershov et al. for the expected benefit of simplified and reliable study of gene polymorphisms as taught by Yershov et al. (Abstract, last 4 lines).

Regarding Claim 13, Cantor et al. teach the hybridized polynucleotide is ligated to the probe (Column 8, lines 8-9).

Regarding Claim 14, Cantor et al. teach the hybridized polynucleotide is ligated to the probe (Column 8, lines 8-9). Cantor et al. do not discuss the reference polynucleotide.

However, reference polynucleotides were known to one of ordinary skill in the art as discussed above and the skilled practitioner would have known that for comparison purposes, a target and reference polynucleotide would be treated equally i.e. ligated to the probe.

Regarding Claim 15, Cantor et al. teach the overhangs have free 5' ends (Column 12, lines 46-49 and Fig. 1B).

Regarding Claim 16, Cantor et al. teach the overhangs have free 3' ends (Column 12, lines 38-45 and Fig. 1A).

Regarding Claim 17, Cantor et al. teach the n-mer comprises from about 4 to 50 nucleotides (Column 12, lines 57-60).

Regarding Claim 18, Yershov et al. teaches the arrays are arranged in parallel (page 4916, left column, second full paragraph).

Response to Arguments

6. Applicant argues that the invention of Claim 12 which recites comparing at least two target hybridization patterns on at least two identical arrays wherein each array constitutes a complete set of n-mers is not *prime facie* obvious over the teaching of Canter et al. alone or in view of Yershov et al. because Canter et al. do not teach determining whether two or more target polynucleotides are identical and because Yershov et al. do not teach probe arrays comprising a complete set of n-mers to analyze mutations. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Cantor et al. teach a polynucleotide array wherein each probe comprises a double stranded region and a single stranded overhang region such that the overhangs in each array constitute a complete set of n-mers (Column 5, line 56-Column 6, line 5) wherein the hybridization pattern is analyzed (Column 7, lines 14-18) and Yershov et al. teach providing at least two identical probe arrays and comparing the hybridization patterns. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the comparison of hybridization patterns as taught by Yershov et al. to the hybridization array comprising a complete set of n-mers as taught by Cantor et al. for the expected benefit of quickly, easily and accurately identifying sequence variations as taught by Cantor et al. (Column 4, lines 5-8).

7. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
April 3, 2001

S. Gromer

STEPHEN G. WALSH
PRIMARY EXAMINER